Chapter 6

Cutaneous Lesions in Cetaceans: An Indicator of Ecosystem Status?

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Additional information is available at the end of the chapter

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1. Introduction

For countless generations, civilization had a relative insignificant impact on the marine environment, particularly on marine mammal species. However, with the dawning of the industrial revolution, a dramatic increase in the utilization of marine species (including whales) as a food source and other industrial purposes resulted in a radical reduction in the numbers of some species during the subsequent years, leading to a notable decrease in marine biodiversity during the 20th century. Fortunately, this exploitation was accompanied by increased awareness and campaigns by environmental and ethical lobby groups, resulting in more controlled and managed whaling activities, which in turn lead to markedly improved whale numbers [1]. However, the tide shifted once again with the dawning of the new millennium, characterized by ever growing industrial development and rapid human population growth. As a result, natural resources came under increased pressure and in particular, development and growth led to the creation of massive amounts of waste and pollutants. Consequently, high levels of marine pollution, especially near urban regions, became a serious threat to the health and well-being of marine mammals, including cetaceans.

The first reports of skin disease in cetaceans date back to the 1950's [2]. However, over the last 60 years the frequency of these reports steadily increased. The question, therefore, arose as to whether scientists are just more aware of this phenomenon and consequently report more cases, or whether the occurrence of these lesions is indeed on the increase. Many natural factors such as ecto-parasites, water temperature and salinity are role players in these diseases. However, anthropogenic impact can no longer be ignored, since these influences can even affect the natural factors by escalating their effect. This brings one to another imperative question; whether these factors are linked, or whether they are merely the result of a coincidence. The aim of this review is therefore, to take a closer look at the

skin of cetaceans, the occurrence of skin lesions among these mammals, the microbes that seem to be the causative agents, as well as contributing factors such as anthropogenic activities.

2. Cetacean skin

2.1. The Barrier: First line of defence

The first study on the anatomy of whale skin was conducted early in the 20th century by Japha [3]. He noted the unusual thickness of the epidermis when compared to other mammals (15 to 20 times thicker as in humans). Later, Parry [4] distinguished between the layers of epidermis, dermis and hypodermis. He differentiated between the epidermal layers and recognised the stratum corneum and the stratum germinativum (Figure 1), consisting of the more superficial prickle cells and the deep cylindrical cells. The hypodermis was found to be thick and fatty, merging into the dermis that consists of white fibres. The dermis stretches into the epidermis by means of 'dermal papillary ridges', and therefore interdigitate with the epidermal papillae (Figure 1) [4]. Parry also studied the vascular system and conductivity of blubber, which affect temperature regulation in these mammals. A few decades later, Sokolov [5] summarized cetacean skin anatomy by stating that the skin of these animals is relatively smooth, and with a ratio of 0.3 - 1.5 % in relation to body length, may reach greater 'absolute thickness' compared to other mammals. He noted that although the stratum corneum is very thick in cetaceans, layers of strata granulosum and lucidum are absent, with the upper layers of the epidermis not fully cornified. Sokolov concluded that sebaceous and sweat glands, as well as pelage, are absent in the skin of cetaceans. Using bottlenose dolphins (*Tursiops truncatus*) as model, it was found that the epidermal layer of cetaceans has a large capacity for cell population and a long turn over time, accompanied by rapid sloughing [6]. These characteristics account for the unusual thickness, as well as the smooth surface of the skin, thereby enhancing the barrier properties and ability to limit attachment by microbes [6, 7].

The stratum corneum of cetaceans (Figure 1) is often referred to as the parakeratotic layer and is composed of moderately flattened cells, characterized by retained elongated nuclei and prominent organelles (including mitochondria), representing a form of parakeratosis [7, 8]. The latter process was attributed to a type of cornification, associated with evolutionary hair follicle loss. The phospholipid-rich cornified layer presumably also aids in waterproofing the skin of these mammals [8]. In addition to these general features of cetacean skin, several unique ultra-structural characteristics were reported for the stratum corneum of the southern right whale (*Eubalaena australis)* [9]. These include lipid droplets occurring in close association with the nucleus, as well as an abundance of intra-nuclear inclusions similar to small fragments of cytoplasmic keratin.

Keratins are scleroproteins responsible for mechanical support in epithelial cells [10]. These macromolecules are mechanically hard, chemically unreactive, insoluble, fibrous, and very tough as a result of the numerous disulfide cross linkages [11]. In terrestrial mammals, keratins are produced by the so-called keratinocytes, found in the stratum basale or

germinativum. The primary function of these keratinocytes, constituting 95% of the epidermis, is to provide a barrier against adverse environmental conditions, such as heat, radiation, water loss and penetration by pathogens. In cetaceans, this barrier is provided by lipokeratinocytes, responsible for the production of both keratin and lipid droplets [12, 13]. These lipids enhance the capability of the lipokeratinocytes to act as physical barrier within a hypertonic environment, and contribute to the unique buoyancy, streamlining, insulation and caloric characteristics of cetacean skin [12]. This physical barrier represents the first line of defence against the environment and prospective invaders.

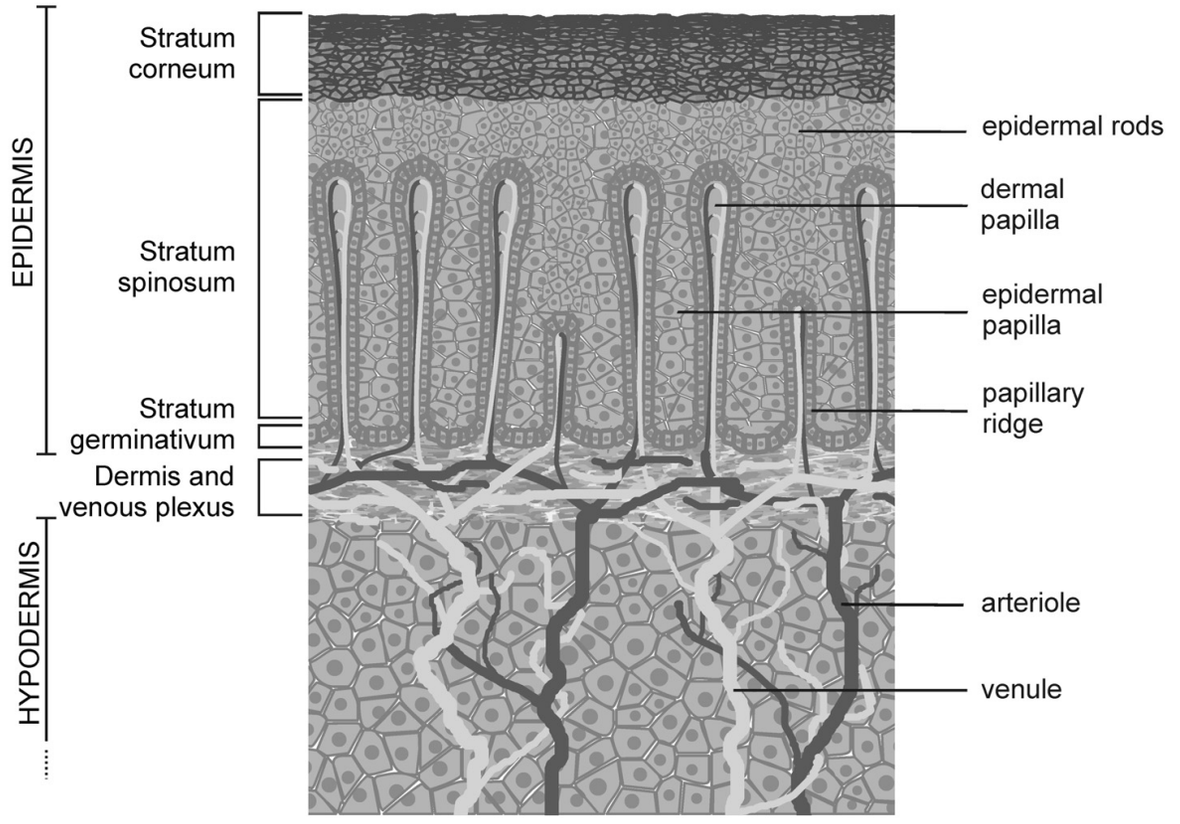

Figure 1. A cross section of cetacean skin, showing the general anatomy of the epidermal, dermal and hypodermal layers (Illustrated according to previous findings [4, 30]; as well as own unpublished data)

2.2. The Barrier: Second and third lines of defence

The primary role of skin is to provide a physical barrier against the environment and this presents the first line of defence. However, crucial immune components form integral elements of the skin, providing the subsequent layers of defence with increasing specificity. Potential microbial invaders will be confronted by the physical, innate (non-specific), chemical and granulocyte barrier (adaptive or specific immune system) that evolved over time to eradicate these invaders, digest invading cells into smaller antigens, and finally to programme lymphocytes in order to provide long term protection against the particular microbe [13].

A microbe that manages to penetrate the subcutaneous layers of the skin will be met by the second line of defence; the innate or non-specific immune system. This defence mechanism involves the production pro-inflammatory substances, such as chemokines by the lipokeratinocytes, resulting in the migration of immune cells such as leucocytes to the site of infection. Leucocytes include among others, the phagocytes (macrophages, neutrophils and dendritic cells). Upon detection of the foreign proteins originating from potential bacterial, fungal or parasitic invaders, Langerhans cells will phagocytise these antigens and migrate to adjacent lymph nodes. In the lymph nodes, these cells will develop into mature dendritic cells which will process the antigen (into smaller fragments), to activate the adaptive immune system (lymphocytes) [14]. On top of this chemical defence mechanism, non-specific antimicrobial substances such as lysozyme and the peptide β-defensin were found in cetacean integument [15]. It was found that lysozyme occurs between the layers of the stratum corneum, within cells of the stratum spinosum, dermis and endothelial cells of the dermal blood vessels. Also, β-defensin was found to be concentrated in the upper five or six layers of the stratum corneum, as well as within the cells of the upper stratum spinosum.

In addition to the above-mentioned non-specific defence mechanisms, intra-epidermal lymphocytes indicate the presence of the adaptive immune system in the epidermis of mammals. These specialized T cells have powerful cytolytic and immuno-regulatory effects on antigens and will confine antigens that overcame the first and second lines of skin defence [14]. Cells associated with this specific or adaptive immune response were also detected in cetacean skin studies [13]. Zabke and Romano [13] reported that their study on dolphin skin revealed the presence of MHC II (+) antigen cells, predominantly situated in the dermal papillae, along the epidermal-dermal border. These cells were found to have a dendritic-like morphology and form patterns, similar to those of Langerhans cells. The latter are known primary antigen presenting cells in the integument of terrestrial mammals, and thus the authors concluded that they were most likely Langerhans cells and not macrophages or dendritic cells. The latter two types were found deeper into the dermis. Zabke and Romano [13] further suggested that pathogen invasion resulting from a wound may lead to an inflammatory response, causing immune cells (neutrophils, macrophages and/or lymphocytes) to migrate from the dermal papillae to the site of infection. However, the authors indicated that inflammation is usually absent in these animals, because this barrier is normally sufficient against small injuries sustained via interactions with other dolphins. The authors further noted that wound healing in dolphins is not accompanied by scab formation. In these mammals hydrophobic changes within in the stratum spinosum, causes rapid sloughing and replacement with cells of the stratum germinativum undergoing mitosis.

From the above it is evident that cetacean skin is an effective physicochemical barrier. To overcome such a challenging obstacle would require a failure of the barrier itself, or creative strategies and unique properties in the prospective invader.

Immune response to cutaneous fungal infections. The type of fungal invader, whether a unicellular yeast or hyphal fungus, as well as anatomical site of infection, will determine the immune response of the host [16,17]. Yeast cells are usually phagocytosed, whereas the

larger size of hyphae prevent them from being ingested. Over time, pathogenic fungi evolved and developed different strategies to survive and even disseminate in mammalian tissue. The neutrophils, macrophages and monocytes are the main antifungal effector cells in the defence strategy, employing shared mechanisms [17]. Firstly, macrophages present at the site of attempted infection, will make an effort to damage or kill the fungus. The second line of defence includes effector cells, the neutrophils and monocytes, which are summoned to the infection site by inflammatory signals from cytokines, chemokines and complement components. These effector cells damage or kill the fungal invader using strategies such as producing reactive oxygen intermediates and antimicrobial peptides [17].

There are four main groups of fungal infections [16]. The first, superficial mycoses, does not provoke any immune response from the host since the fungus would only grow on compounds associated with the skin. The remaining three categories provoke immune responses and include cutaneous, subcutaneous and deep mycoses. In cases of local trauma, subcutaneous mycoses may develop with the subcutis as the primary site of infection. In such cases, leucocytes and eosinophils will respond, leading to the formation of cysts or granulomas. Deep mycoses usually occurs in immuno-suppressed mammals, with entry through the lungs, paranasal sinuses, digestive system, or mucous membranes. Total fungal dissemination is usually a sign of severe immune failure.

3. Microbes – The enemy?

A limited number of organisms have the ability to degrade and utilize keratin, the key structural component of mammalian skin [18]. These include a few insect species, as well as a number of bacteria and fungi. Higher vertebrates are also not known to digest keratin [11]. Microbes degrade keratin by the secretion of extracellular proteolytic enzymes, known as keratinases; members of the serine proteinase group of enzymes [19, 20]. These enzymes are robust with a wide temperature and pH activity range, and have the ability to hydrolyze both natural and denatured keratin [21]. Keratinases from the fungus *Microsporum gypseum* were found to cleave the disulfide bridges in the keratin (sulfitolysis), which were followed by a further attack on the keratin structure by extracellular proteases [18]. Tsuboi and co-workers [22] found a keratinolytic proteinase in another fungus, i.e. *Trichophyton mentagrophytes*, with an optimal pH of 4.5 for keratin and 3.9 for haemoglobin. They showed that this fungus could potentially invade healthy skin (with a weakly acidic pH), by breaking down the keratin and thereby making it possible for the organism to invade the stratum corneum. This ability to degrade keratin, and other molecules associated with skin, can be regarded as a putative microbial virulence factor [20].

Keratinophilic (keratin loving) fungi (Figure 2) represent the largest group of organisms with the ability to degrade and utilize keratin as a source of carbon and nitrogen [11, 16]. These fungi commonly occur in soil and sewage sludge, which contain high concentrations of keratin remnants with specific physiochemical properties and associated microbial populations [23]. Releasing sewage sludge into the environment, or using it for fertilizing purposes, can therefore lead to spreading of potentially pathogenic fungi into new

ecosystems. Plants, humans and animals are subsequently exposed to a variety of potentially infectious microbes. Fungal genera known to harbour keratinophilic species include: *Acremonium, Alternaria. Aspergillus, Candida, Chaetomium, Chrysosporium, Cladosporium, Curvularia, Fusarium, Geotrichum, Gliocladium, Gymnoascus, Microsporum, Monoascus, Mucor, Paecilomyces, Penicillium, Scopulariopsis, Sporothrix, Trichoderma, Trichophyton,* as well as *Verticillium* [16, 23-25].

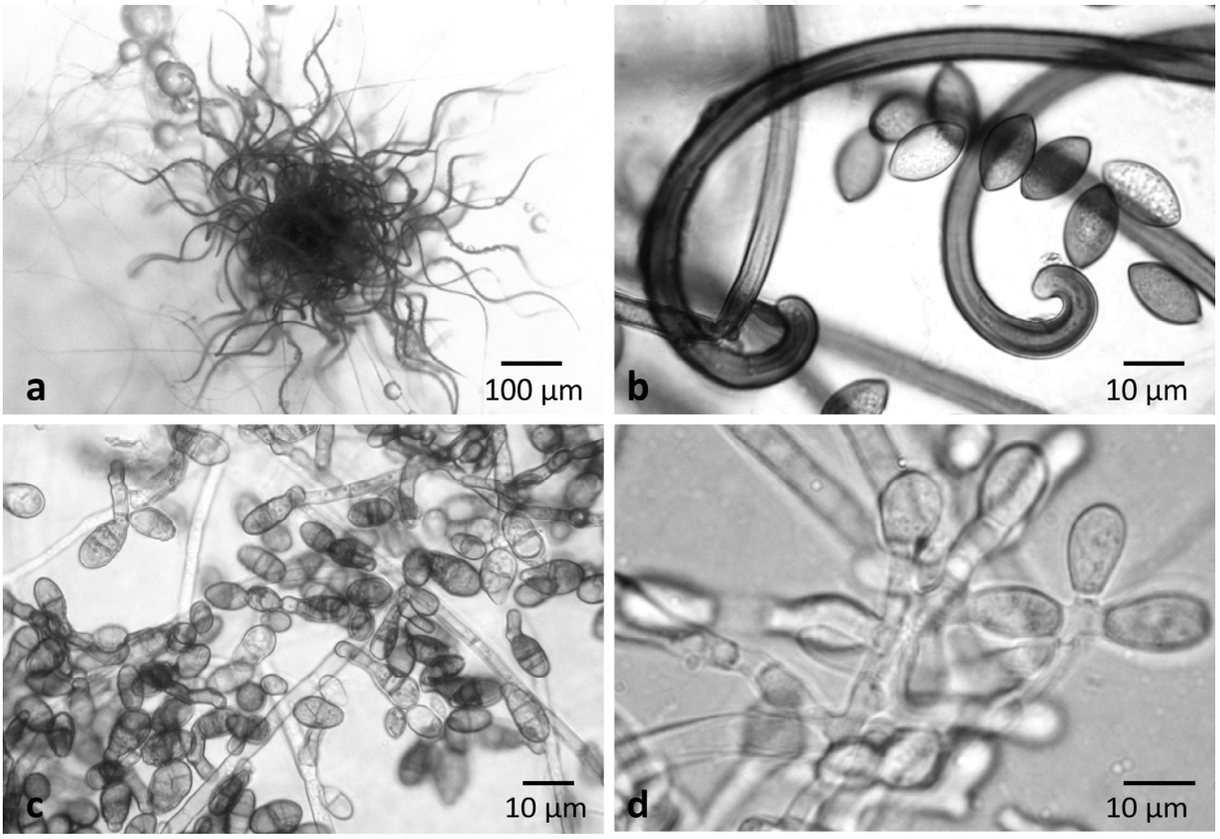

Figure 2. Light micrographs of keratinophilic fungi. a. Fruit body of *Chaetomium murorum* with long ascomatal setae; b. ascomatal setae and ascospores of *Chaetomium murorum*; c. conidia of *Alternaria alternata*; d. Fertile hyphae of *Chrysosporium keratinophilum* bearing conidia

Some keratinophilic fungi (Figure 2) are known to be pathogenic, and often the cause of cutaneous skin infections. These include the so-called dermatophytes, belonging to the genera *Epidermophyton, Microsporum* and *Trichophyton,* as well as non-dermatophytes such as *Aspergillus, Candida, Fusarium* and *Scopulariopsis* spp. Moreover, De Hoog et al. [16] remarked that more cases of fungal infections seem to be caused by fungal spp. formerly known as being saprobic, and appear to be associated with the increasing numbers of immuno-compromised patients. These fungi are mostly opportunists that cause infection when the immune system of the host is breached [16, 17]. Interestingly, of more than 100 000 known fungal species, only about 100 have been reported regularly, as infectious agents of animals, as well as humans [16].

Certain species of the bacterial genus *Bacillus* also have the ability to produce keratinases. *Bacillus cereus, Bacillus licheniformis* and *Bacillus subtilis* have been identified and studied in

this regard for commercial purposes, specifically for the biodegradation of feathers in the poultry industry [21, 26]. Other bacterial genera with keratinolytic ability include: *Lysobacter, Nesternokia, Kocurica, Microbacterium, Vibrio, Xanthomonas, Stenotrophomonas* and *Chryseobacterium* [24].

4. Case studies of skin lesions in cetaceans – The signs?

Skin lesions in cetaceans have been reported since the 1950's [2]. Some examples of the steady stream of reports in later years are presented below.

Skin lesions containing *Staphylococcus* were reported for the first time in cetaceans in 1988 [27]. In that study, two isolates of *Staphylococcus* were obtained from purulent tissue that occurred in two captive dolphins with multiple, suppurating lesions, and subsequently described as a new species, *Staphylococcus delphini*.

A study conducted over a four year period found that a range of microbes were associated with lesional and non-lesional skin in a group of bowhead whales (*Balaena mysticetus*), characterized by dozens to hundreds of roughened areas on their skin surfaces [28]. The majority of microbes, isolated during the study, were associated with the lesional skin: 56% of Gram positive bacteria, 75% of Gram negative bacteria and 64% of the yeasts. Also, the lesional skin was characterized by the presence of *Corynebacterium* spp., *Acinetobacter* spp., as well as representatives of *Moraxella*. *Candida* spp. were the dominant yeast species, followed by representatives of *Cryptococcus* and *Rhodotorula.* Subsequent tests on the isolates showed the production of enzymes able to cause necrosis by microbes originating from both lesional and non-lesional skin. These whales occurred in regions with increased industrial activities (gas and oil exploration) in the Beaufort Sea; the authors speculated that the roughened skin areas might have been associated with the adherence of spilled oil [28].

A study examining skin diseases among wild cetaceans from British waters found 69% of individuals to be affected [29]. The authors reported wounds and other traumatic injuries, as well as lesions caused by pox and herpes viruses, as well as bacteria, ectoparasites and non-specific ulcers. Concerns that the lesions were associated with pollution were raised but not confirmed [29].

Henk and Mullan [30] examined 23 bowhead whales and reported shallow lacerations, circular depressions and epidermal sloughing on these whales' skin. The authors also found abundant bacteria and diatoms associated with these lesions, and even higher numbers where the stratum spinosum was exposed. The bacterial isolates were found to include cocci, bacilli and filamentous spp., with increasing numbers associated with higher levels of necrotic decay. Protozoa and fungi were also observed and also increased in incidence with more disturbed epidermal surfaces. The authors also identified several erosive enzymes from these microbes and suggested an association between the whales' skin and spilled oil.

A pygmy sperm whale (*Kogia breviceps*) and an Atlantic white-sided dolphin (*Lagenorhynchus acutus*) were reported with mycotic dermatitis, in the form of raised, firm, erythemous, cutaneous nodules on parts of their bodies [31]. The dermatitis cases were the result of

infections caused by a species of *Fusarium*, and in both cases, the disease was preluded by stress factors, such as stranding, which presumably induced immuno-suppression.

Resident bottlenose dolphins, from the Sado estuary in Portugal, were examined and 85% of the community showed signs of skin disorders [32]. The authors compared these results to observations from other areas, and came to the conclusion that habitat degradation played a significant role in these disorders since eutrophication seemed to a serious problem in this estuary. Consequently, the authors attributed these conditions to apparent depressed immune systems caused by stress, habitat degradation and pollution.

Ten coastal populations of bottlenose dolphins served in a photographic study that compared levels of epidermal disease among populations exposed to a wide range of natural and anthropogenic conditions [33]. It was found that epidermal lesions were common in all populations. However, the severity and prevalence of the different classes of lesions, varied among the populations. Those occurring in areas with lower water salinity and temperature had a higher lesion incidence and severity. On the other hand, no direct correlation was found between the lesion characteristics and toxicology data. The authors concluded that the oceanographic variables might influence the epidermal integrity of the skin or cause physiological stress, thereby rendering these mammals more prone to natural infections or impact by anthropogenic activities.

In 2001, Mikaelian and co-workers [34] reported a case of six beluga whales (*Delphinapterus leucas*) with slightly depressed, greyish round lesions, found dead on the shores of the St. Lawrence estuary. Histology of the lesions revealed *Dermatophilus*-like actinomycetes that had invaded the stratum corneum of the epidermis [34]. Even the stratum spinosum of these animals were characterized by marked spongiosis and vacuolar degeneration. These whales were furthermore free from ectoparasites, thereby eliminating the possibility of this predisposing factor. Immunodeficiency seemed to be the most likely cause of these *Dermatophilus*-like infections, since four of the six individuals were characterized by chronic debilitating diseases. Martineau [35] followed this up by reporting on an extensive survey (1983-1999) on the beluga whales from this estuary. They found cancer rates in these animals to be much higher than in any other population of cetaceans, similar to that of other mammals (including humans) from the same area. They believed that environmental contaminants, such as polycyclic hydrocarbons (PAH) were involved in the aetiology of these conditions.

A visual health assessment study in North Atlantic right whales (*Eubalaena glacialis*) revealed a variety of skin conditions, as well as the calving intervals in these mammals increasing from 3.67 to 5 years, thereby significantly impacting on the population growth [36]. The authors speculated that possible causes might include environmental contaminants, marine bio-toxins, nutritional stress, genetic influences, as well as infectious diseases.

Hamilton and Marx [37] presented results of a study conducted from 1980 until 2002 on skin lesions among North Atlantic right whales. The authors documented white, blister, swath and circular lesions. White lesions appeared to represent episodic events, the incidence of blister lesions were more constant, whereas swath lesions were often associated with fatal conditions. They reckoned that skin lesions are indicators of compromised health, possibly caused by deteriorating habitat quality in coastal areas.

Between the years 2006 and 2009, Van Bressem and co-workers published extensively on many cases of skin lesions in a range of cetaceans. In one such study [38], the authors examined 'tattoo' skin lesions caused by poxvirus infections in four species of small cetaceans (*Lagenorhynchus obscurus, Delphinus capensis, T. truncatus* and *Phocoena spinipinnis*) near Peru. They reported a possible increase in the disease since 1990 in two of the species (*L. obscurus* and *P. spinipinnis*). They also found that male *P. spinipinnis* individuals were two times more infected than their females [38].

A population of long-beaked common dolphins (*D. capensis*) was studied between 1985 and 2000 in the Southeast Pacific near Peru, characterised by extensive fisheries activities [39]. The authors reported the presence of a variety of cutaneous lesions, abnormalities and scars, on between 1.8% and 48.2% of these dolphins. Tattoo lesions, punctiform and round marks, dark circle lesions, coronet marks and abnormal pigmentation were described, among many other abnormalities in this population. These lesions were attributed to pox- and herpes viruses, as well as other unknown viruses and parasites.

An extensive survey conducted from 1984 until 2007 and dealing with previously unreported cases of skin and skeletal diseases in cetaceans from Ecuador, Colombia, Peru, Chile, Argentina, Uruguay, Brazil and Venezuela, was presented as an overview in 2007 [40]. The authors reported tattoo skin disease, lobomycosis-like disease and other cutaneous infections with unknown aetiology in 590 cases, out of a total of 7635 specimens, including 12 different odontocete spp. that were examined. It was suggested that anthropogenic factors, including aquaculture, fish factories, untreated waste water, ballast water and chemical pollution, play a major role in the degradation of the habitats of these cetaceans, thereby contributing to the poor health status of many individuals in these populations.

Chronic mycotic disease of the skin and subdermal tissues in Indo-Pacific bottlenose dolphins (*Tursiops aduncus*), caused by the fungus *Lacasia loboi,* was reported in 2009 [41]. These dolphins lived in the tropical lagoon of Mayotte, situated in the Indian Ocean between Mozambique and Madagascar, and were characterized by numerous raised, greyish nodules on the head, flanks, dorsal fin, belly, back and tail. In some individuals, the lesions appeared to be quite severe and lesions resembling other unknown fungal infections were also observed. Habitat degradation, especially along the coastal areas where rapid urbanization, agricultural activities and untreated waste water are evident, was mentioned as a contributing factor to the aetiology of the disease.

Inshore and offshore surveys conducted, from 1997 to 2007, on bottlenose dolphins in the larger Santa Monica Bay, California, revealed a very high incidence and extent of skin lesions [42]. Causative agents found included bacteria, viruses, fungi, vitamin deficiencies, diatom growth and parasites. However, anthropogenic activities were thought to be a major contributing factor and seemed to be linked to especially viral outbreaks. Moreover, this area (the Southern California Bight) is known for high concentrations and volumes of pollutants entering the coastal and offshore environment, as well as contaminated sediments that cover a 44 km^2 on the ocean floor, containing dichloro-diphenyl-trichloro-ethane (DDT) and polychlorinated biphenyls (PCBs).

A study conducted during 2006 and 2007 revealed notable differences in skin diseases between two communities of Guiana dolphins (*Sotalia guianensis*) from Brazil [43].The authors found that the community, living in the chemically and biologically polluted Paranaguá estuary, was characterized by the occurrence of lobomycosis-like and nodular skin diseases. This estuary is known for its high levels of chlorinated hydrocarbons, as well as regular oil spills. In contrast, another community of Guiana dolphins, living in the less polluted Cananéia estuary, was free from these skin diseases and had relatively low tissue levels of organochlorines. The authors consequently proposed that lobomycosis-like and nodular skin diseases might act as indicators of environmental burden.

A southern right whale neonate that beached along the Southern coast of South Africa and suffering from extensive skin lesions were found to be infected with a number of cutaneous fungi including *Chaetomium globosum, Chaetomium murorum* and *Penicillium coprophilum* [44]. During the same period, another southern right whale neonate was found beached and suffering from a yeast infection caused by *Candida zeylanoides* [45]. In both cases the authors speculated about anthropogenic factors contributing to the condition of the animals.

Maldini and co-workers [46] reported on bottlenose dolphins living in Monterey Bay, California. Their research, conducted between 2006 and 2008, showed that approximately 90% of these cetaceans were characterized by skin lesions. They identified five skin conditions, with pox-like lesions being the most frequently found. The authors suspected that contaminants such as persistent organic pollutants (POPs) and heavy metals were contributing factors that weakened the immune systems of the dolphins, thereby rendering them more susceptible to viral infections.

A recent study on North Pacific humpback whales (*Megaptera novaeangliae*) examined bacterial species associated with the skin of these mammals [47]. It was found that healthy individuals were characterized by similar microbial communities, as opposed to health-compromised individuals that harboured different populations. Also, the microbial populations on the skin of these animals were found to be different to that of the seawater, which led to the conclusion that the skin-associated bacteria were adapted to live on the epithelium and its constituents. The study also reported that the bacterial phylum found most on healthy individuals is Bacteroidetes, in contrast to the health-compromised individuals which harboured Gammaproteobacteria as the dominant group.

Cetaceans are also exposed to UV radiation and often exhibit lesions similar to skin cancer in humans [48]. Interestingly, cetacean species with darker pigmentation have less UVR induced skin damage. Also, latitude affects the incidence of this phenomenon, since UVR dosage at lower latitudes, are 5 times higher than at mid-latitudes.

A recent study by Fury and Reif [49] reported poxvirus lesions in two estuarine populations of bottlenose dolphins from Australia. This was the first report of poxvirus-like lesions in Australian cetaceans. Their results suggested that these infections were accompanied by climatic events, such as flooding in this case, which lead to lower water salinity and higher occurrence of dolphin pox. They concluded that diseases such as dolphin pox, might act as indicators of environmental stress.

It seems evident from the above mentioned studies that the occurrence and high prevalence of skin lesions in many cetacean populations are linked to environmental factors, including water salinity and temperature, as well as pollution and eutrophication. These skin lesions may be caused by a wide diversity of microbes that will be discussed in the next section.

5. Microbes causing skin lesions in cetaceans

5.1. Virus infections of cetacean skin

5.1.1. Dolphin pox

Poxviridae represent the largest family of viruses known to cause diseases in marine and terrestrial mammals [50]. Among cetaceans, the odontocetes seem to be more affected than the mysticetes [49]. Species of cetaceans reported to be affected by pox viruses, include Atlantic bottlenose dolphins [7, 50], bottlenose dolphins from Australia [49], Atlantic white-sided dolphins [7, 50], common dolphin (*Delphinus delphis*), dusky dolphins, white-beaked dolphins (*Lagenorhynchus albirostris*) [29, 50], striped dolphins (*Stenella coeruleoalba*) [29, 50], Hector's dolphins (*Cephalorhynchus hectori*) [7, 29, 50], long finned pilot whales (*Globocephala melaena*) [29, 50], as well as a few spp. of porpoises [50].

Dolphin pox has been associated with a variety of lesions, referred to as 'targets', watered-silk', 'ring', 'pinhole', 'circle' and 'tattoo'-like [7]. These lesions emerge as single or overlapping circular grey spots. Later, these ring lesions may develop into black punctiform stippled patterns. Histological studies revealed a thickened stratum corneum with ballooning degeneration, and eosinophilic inclusions containing virus particles, inside the cytoplasm of stratum intermedium cells. Studies on this disease pointed to one consistent feature; its relationship with compromised environmental conditions and consequent general health of affected individuals [7, 51].

5.1.2. Herpes virus

Herpes virus had been reported as the causative agent of focal dermatitis in captive, as well as free-swimming beluga whales [51, 52]. Lesions caused by this virus appeared as multiple grey, raised, pale grey regions on the skin, which eventually ulcerated and healed very slowly. At the time of infection, these whales appeared to be in poor health and under stress. Histological analyses showed epithelial cells that underwent intercellular oedema, necrosis and the development of microvescicles. Prominent eosinophilic, intra-nuclear, inclusion bodies were evident in infected epithelial cells [51].

5.1.3. Papillomavirus in cetaceans

In cetaceans, papillomas have been reported on the skin, as well as the tongue, penis, pharynx and first gastric compartment [51].

5.1.4. Calicivirus induced vesicular disease

Smith and co-workers [53] reported an Atlantic bottlenose dolphin with vesicular skin disease caused by calicivirus. This disease was apparently transferred to another dolphin, but via a sea lion. The lesions eventually eroded and left shallow ulcers. Interestingly, serological studies on mysticete spp. from the North Pacific, showed the presence of neutralizing bodies to several marine vesiviruses, including calicivirus [54].

5.2. Bacterial infections of cetacean skin

A variety of bacteria have been reported from skin lesions in cetaceans. These include species of *Brucella, Corynebacterium, Dermatophilus, Escherichia, Erysipelothrix, Klebsiella, Mycobacterium, Pseudomonas, Staphylococcus, Streptococcus* and *Vibrio* (Table 1) [27, 47, 55]. Bacteria also cause death of cetaceans in many cases [55]. However, it must be noted that these infections are usually of a secondary nature and occur as a result of other stresses, such as parasites and immuno-suppression following exposure to toxins.

Bacterial genus	Bacterial species occurring on cetaceans
Brucella	*Brucella cetacea* had been reported from sub-blubber abscesses in several species of cetaceans [56]. Also, *Brucella ceti* had been isolated from subcutaneous and skin lesions in cetaceans [57].
Corynebacterium	A species of *Corynebacterium* had been isolated from skin lesions in an Atlantic bottlenose dolphin [55].
Dermatophilus	Lesions caused by *Dermatophilus*-like actinomycetes were observed in six deceased beluga whales that were found in the St. Lawrence estuary [34]. These lesions presented as slightly depressed, round and grey areas on the skin.
Enterobacter	*Enterobacter agglomerans* had been reported from skin lesions on an Atlantic bottlenose dolphin from Florida, USA [55].
Escherichia coli	*E.coli* isolates were obtained from skin lesions on Atlantic bottlenose dolphins from Florida and New York, USA [55].
Erysipelothrix	*Erysipelothrix rhusiopathiae* had been reported as the cause of skin disease in dolphins, characterized by dermal infarction causing dermal sloughing [51]. This disease is usually subacute and chronic in cetaceans or acute septicaemia [56]. As a small, pleomorphic, Gram positive rod, this bacterium is a commonly found in the mucous of fish, suggesting that the dolphins become infected by ingesting these fish [51, 56, 58, 59]. Injuries caused by the teeth of other cetaceans, is another possible route of infection [56].
Klebsiella	*Klebsiella oxytoca* was isolated from skin lesions of an Atlantic bottlenose dolphin, while another *Klebsiella* sp. was obtained from a goosebeak whale (*Ziphius cavirostris*), both from Florida (USA) [55].

Bacterial genus	Bacterial species occurring on cetaceans
Mycobacterium	Species of *Mycobacterium* have been associated with infections in cetaceans, including bottlenose dolphins, belugas and pseudorca's. In the infected animals, non-healing, chronic cutaneous or subcutaneous lesions were present and associated with other symptoms, such as granulomas in various organs and lymph nodes, as well as pulmonary infections [56].
Pseudomonas	This genus is known for Gram negative, motile, slender bacillus bacterium cells, and generally occurs in water. These bacteria often colonize wounds, which can lead to septicaemia [14]. *Pseudomonas aeruginosa* had been reported to form large cutaneous ulcers in Atlantic bottlenose dolphins, penetrating deep into the tissue and consequently leading to serious conditions in the affected animals. Septicaemia develops when the bacteria proliferate into the walls of the blood vessels [56]. A *Pseudomonas* sp. and *Pseudomonas putrefaciens,* had also been isolated from skin lesions in Atlantic bottlenose dolphins by Buck and co-workers [55].
Staphylococcus	A new species in this genus, *Staphylococcus delphini,* was described by Varaldo and co-workers [27]. Moreover, this represented the first report of an association between this genus and cetaceans. *S. delphini* isolates were obtained from suppurative skin lesions in two captive dolphins which recovered rapidly after antibiotic treatment [27].
Streptococcus	*Streptococcus* bacteria are Gram positive diplococci and common residents of cetacean's skin and upper respiratory tract. Cutaneous infections caused by these species, are therefore usually opportunistic and associated with animals under stress of some sort [51]. Species from this genus have been isolated from cetaceans with skin lesions [55], septicaemia, metritis and pneumonia. Amazon River dolphins have been reported with a specific dermatological condition, commonly known as 'golf ball disease', caused by *Streptococcus iniae*, and characterized by the presence of slow-growing, nodular, subcutaneous abscesses [56].
Vibrio	Buck and co-workers [55] found that *Vibrio* spp. were the most commonly isolated bacteria from stranded cetaceans. The two species specifically associated with skin lesions, were *Vibrio alginolyticus* and *Vibrio parahaemolyticus* originating from Atlantic bottlenose dolphins (*T. truncatus*) from Florida and New Jersy (USA). Dhermain and co-workers [58] also implicated bacteria from this genus, in cases of cetacean septicaemias.

Table 1. Bacterial species reported to cause skin lesions in cetaceans

5.3. Fungal infections of cetacean skin

5.3.1. Candida

Species of *Candida* are commonly associated with the mucous membranes of animals in limited numbers, and occur predominantly in the regions of the blowhole, oesophagus, vagina and anal area in cetaceans [59-61]. *Candida* spp. reported from cetaceans include *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida tropicalis*, *Candida parapsilosis*, *Candida guiliermondii*, *Candida lambica* and *Candida ciferrii* [59, 60]. *Candida zeylanoides* was also found to be associated with the skin of a southern right whale neonate from South Africa [45]. Infections caused by *Candida* spp. mostly affect captive cetaceans and are usually associated with immuno-suppressed individuals, where the *Candida* infection may proliferate and cause severe local infection of the skin or mucosal membranes. In captive cetaceans, infections are usually observed after long-term antibiotic therapy [30, 61], but had also been reported following corticosteroid treatment of the animals, as well as after overtreatment of tank water [59]. These lesions usually occur as whitish, creamy plaques on the skin or mucosal surfaces. Histological examinations usually show colonies of pseudohyphae, septate hyphae and blastospores [16, 60].

In cutaneous *Candida* infections, the skin or mucosal membranes, may suffer acanthosis (hyperplasia and thickening of the stratum spinosum) with pseudoepitheliomatous hyperplasia, with the fungus growing in the epithelial tissue. These cutaneous *Candida* infections had been reported in a number of cases pertaining to especially captive cetaceans and varied from ulcerative dermatitis, to inflammation without ulcers and healed ulcers. However, significantly more cases of visceral lesions and systemic candidiasis had been reported in these mammals [60].

5.3.2. Fusarium

Fusarium spp. are well known saprophytes in soil, as well as the cause of a range of plant diseases. However, they also often cause hyalohyphomycosis after traumatic inoculation in humans and seem to be an emerging pathogen in immuno-compromised patients [16]. In cetaceans, mycotic dermatitis caused by a *Fusarium* sp., was reported in a pygmy sperm whale and an Atlantic white-sided dolphin. These cetaceans were characterized by elevated, firm, erythematous, cutaneous tubercles mostly found on the heads, trunks and caudal portions of the cetaceans' bodies [31].

5.3.3. Lacazia loboi

The yeast-like, dimorphic fungus, *Lacazia loboi* (formerly known as *Laboa loboi*) causes invasive cutaneous lesions in dolphins and humans [58], known as lobomycosis, lacaziosis or keloidal blastomycosis [41, 59, 62]. The first case of keloidal blastomycosis was described in 1931 in a human patient from the Amazon valley [63]. This disease was only known to affect humans until 1971, when Migaki and co-workers described a case of lobomycosis in an Atlantic bottlenose dolphin [64]. In 1973, De Vries and Laarman [63] described another

case of this disease in a Guinana dolphin. Interestingly, no other cetaceans other than dolphins have ever been reported with this disease [59, 60]. It is generally accepted that the disease is the consequence of injuries sustained by the animal [61], and can therefore be transmitted to humans during necropsies [58]. It presents itself as white, elevated, crusty, nodular lesions on the animal's body [59-61], although mainly on the head, flippers, abdomen, fins, back tail stocks and flukes [60]. On cellular level, the disease presents with superficial granulomatous dermatitis, associated with macrophages and multinucleated giant cells containing a variety of round yeast cells [61]. More cases of this disease affecting cetaceans have been added to the list and recently some authors suggested that the incidence of lobomycosis might represent opportunistic infections in immuno-compromised hosts [62, 65]. The bio-accumulation of environmental contaminants in the affected dolphins was thought to possibly contribute to susceptibility to this disease [62].

5.3.4. Dermatophytes

Dermatophytes are fungi that grow on the outermost layers of the skin of animals, including muco-cutaneous membranes, genitalia, external ears, as well as dead skin or hair. Ringworm presents one type of dermathophyte and includes the genera *Tinea, Trichophyton, Epidermophyton* and *Microsporum* [16]. Infections caused by dermatophytes, seem to be rare in marine mammals, and therefore also in cetaceans. Limited reports include discrete nodules on the back of a captive Atlantic bottlenose dolphin caused by a sp. of *Trichophyton* [60].

6. Marine pollution and the impact of industrialization on cetaceans – A possible cause?

Rapid population growth and industrialization have characterized urban development. However, the rate of population growth is far higher than the rate of waste and wastewater infrastructure planning and development [1, 66]. This phenomenon has led to ever increasing pressure on natural resources and the creation of massive volumes of waste and waste water [67]. Marine pollution had been defined as deleterious effects resulting, either directly or indirectly, from the introduction of substances or energy by humans to the marine environment [66]. High levels of marine pollution especially along urban areas, pose a serious threat to the health of humans, as well as marine mammals. Although numbers of cetaceans have markedly improved over the past few years as a result of conservation efforts, the quality of the habitat in and near bay areas are critical, because these areas are used by these marine mammals for feeding, mating and calving [1]. Waste entering the marine environment had been categorized into the following groups of activities [68]:

- Waste from land-based sources such as sewage and industrial effluent discharges, storm-water run-off, agricultural and mining return flows, as well as seepage from contaminated ground water. These account for the highest percentage of waste to enter the sea environment.
- Atmosphere pollutants, including persistent organic compounds from vehicle exhausts and industries.

- Waste from ships, oil spills and the discharge of ballast water, as well as other waste.
- Dumping at sea, e.g. dredge spoil.
- Offshore exploration, e.g. oil exploration platforms.

6.1. Human waste into the marine ecosystem

There are 33 megacities in the world, and 21 of them are situated on coastlines. If one considers that at least 50% of the world's population lives in urban areas, where wastewater management systems are often outdated or completely inadequate, the sensitive urban coastal ecosystems are under serious threat [66]. It is estimated that over 90% of wastewater in developing countries is discharged, without any form of treatment into the marine environment, as well as into rivers and lakes. In more developed countries, at least primary treatment is required before discharging wastewater into the environment. Consequently, millions of litres of raw waste water or digested sludge are released into the marine environment. This practice often represents an alternative to tertiary treatment, as well as the most inexpensive means of disposal. The effluents released in ocean outfalls contain faecal material from domestic waste water and industrial discharges with persistent toxic substances and heavy metals. Harmful impacts include risk to public health, beaches, marine animals, as well as contamination of shellfish. Moreover, this release of high volumes of organic matter into the marine environment or contributory rivers also results in eutrophication, which leads to so-called dead zones in the seas and oceans. Approximately 245 000 km^2 of marine environment is thought to be affected by these dead zones [66, 69].

Bitton's [69] book summarized several global surveys of enteric pathogens in contaminated sea water. A number of authors reported enteric viruses of the coast of countries such as Brazil, France, Israel, Italy, Spain and the USA. The virus types found included polioviruses, coxsackie A and B viruses, echo-, adeno- and rotaviruses. These were also detected in sediments in close proximity of sewage outfalls, and found to prevail for extended periods of time. Also, pathogenic bacteria such as *Salmonella* and *Vibrio cholerae* were reported in coastal waters near ocean outfalls. Several illnesses among the human population have been reported as a result of exposure to bacteria from sewage contaminated water, including spp. of *Aeromonas, Leptospira, Mycobacterium, Legionella, Pseudomonas, Vibrio* and *Staphylococcus.* Adenoviruses were also associated with these illnesses, as well as the protozoa, *Naegleria fowleri* and *Acanthamoeba.* These microbes were found in cases of wound infections, skin and subcutaneous lesions, dermatitis, subcutaneous abscesses, septicaemia, conjunctivitis, pharyngitis, meningoencephalitis, Legionnaire's disease and ear infections. Outbreaks of gastroenteritis, on the other hand, were attributed to *Giardia* and *Cryptosporidium,* as well as *E. coli, Shigella* and gastroenteritis of unknown origin.

Some autochthonous microbes have also been documented as agents of disease among humans. *Pseudomonas aeruginosa,* for example, had been reported in immuno-compromised patients, and was also detected in high numbers in faecal polluted recreational waters [69]. Utilizing such recreational areas, was found not only to be associated with enteric diseases, but also with upper respiratory infections. Cases of pneumonia have been attributed to

Staphylococcus aureus, *Pseudomonas putrefaciens*, *Aeromonas hydrophila* and *Legionellae pneumophila.* Cases of skin infections were found to be caused by opportunistic spp. of *Aeromonas*, *Mycobacterium*, *Staphylococcus* and *Vibrio*, after swimming in contaminated recreational waters.

Sewage pollution may also influence the diversity of potential fungal pathogens that are known to infect humans and animals. Keratinophilic microbes occur in high numbers in sewage sludge since it contains high concentrations of keratin remnants [16]. These fungi, including the so-called dermatophytes are known as causative agents of a wide variety of cutaneous and subcutaneous mycoses. Awad and Kraume [23] found the following fungal species, retained in the following genera, in aerobic and anoxic sludge from wastewater plants in Berlin, Germany: *Chrysosporium, Microsporum, Trichophyton, Acremonium, Alternaria, Aspergillus, Candida, Chaetomium, Cladosporium, Fusarium, Geotrichum, Gliocladium, Gymnoascus, Mucor, Paecilomyces, Penicillium, Scopulariopsis, Sporothrix, Trichoderma* and *Verticillium.* It has been stated that the release of these fungi into the environment via activated sludge, presents an indisputable health risk [11, 23].

6.2. Heavy metals

Heavy metals are metallic chemical elements with a relatively high density and are also known as 'toxic metals'. This group includes elements such as copper (Cu), zinc (Zn), lead (Pb), mercury (Hg), nickel (Ni), cobalt (Co), arsenic (As), thallium (Tl) and chromium (Cr). These metals are common components of the earth's crust and occur naturally in ecosystems at different concentrations. However, the bio-available concentrations of these elements have increased significantly over time since the dawn of the Industrial Revolution. The resulting bio-accumulation of these metals has reached critical levels in many ecosystems. These elements enter the water supply through industrial and consumer waste, or acidic rain that in turn causes chemical reactions in soil releasing the metals into streams, rivers and ground water. Additional sources include waste from chemical, electro-plating, tanning, smelting and especially the mining industry [70]. Previously, the lead added to motor fuels as an anti-knock agent was released on large scale into the atmosphere in exhaust fumes with a substantial proportion settling on road surfaces. Run-off water from these surfaces therefore contained high levels of lead. Urbanized and heavy industrialized areas are consequently the foci of heavy metal pollution [71].

Living organisms require small amounts of certain heavy metals or trace elements for normal metabolic processes, in the form of co-factors in enzymes. Some heavy metals such as Cd, As, Pb and Hg pose the biggest threat to the health of humans and animals, and daily intake of these metals are toxic and often fatal. Long-term exposure of humans to As in drinking water for example, had been reported to cause increased risk to skin and other types of cancer, as well as other skin lesions including hyperkeratosis and pigmentation anomalies. Similarly, Cd exposure is associated with kidney damage and increased incidence of bone fractures [70]. Marine mammals often occupy the top levels of marine food chains, and therefore, heavy metals accumulate in these animals [72]. In water, heavy

metals may be found in solution in the water column, as colloids, as suspended particles or absorbed to particulate matter [71]. The latter form often ends up as a constituent of the sediment and at least a portion is released again into the water column. It is also important to realize and take into account that not all sources of heavy metals are anthropogenic. The Mediterranean Sea for example is known for its natural high levels of Hg, and likewise the Arctic Sea for higher cadmium (Cd) concentrations [72]. Furthermore, different organs tend to accumulate different heavy metals, and are therefore metal specific. Heavy metals enter cetaceans through their lungs, skin (absorption), from the mother during gestation, through milk during nursing, as well as by ingestion of sea water and food. Also, mysticetes seem to be less affected by heavy metal accumulation as a result of their position in the food chain, when compared to odontocetes that occupy the top level. Interestingly, heavy metal levels are higher in older individuals and non-breeding females. All these factors should be taken into account in studies on the effects of these metals on marine mammals.

A recent multi-factorial study [73] on mass stranded sperm whales (*Physeter macrocephalus*) revealed relatively high levels of environmental pollutants, including organic Hg (MeHg), Se, Cd, with a Hg:Se ratio of 1:1. Also, opportunistic bacteria cultured from selected organs included representatives of *Vibrio*, *Aeromonas hydrophila* and *Enterococcus*. The authors concluded that these whales were presumably starved causing the mobilization of lipophilic contaminants which accumulated in the adipose tissue. These chemical compounds entered the blood circulation causing immuno- and neurotoxic effects which led to impaired orientation and space perceptions in these sperm whales [73].

6.3. POPs

It is a generally accepted fact that that persistent organic pollutants (POPs) cause harm to human and animal tissue, earning them a reputation of 'the most widespread and toxic group of pollutants', as well as 'poisons without passports' [74-78]. Humans and animals worldwide were found to be carriers of POPs; from trace up to harmful amounts in their bodies [79-81]. Persistent organic pollutants include the chlorinated pesticides aldrin, dieldrin, dichlorodiphenyltrichloroethane (DDT), endrin, heptachlor, hexachlorobenzene, mirex and toxaphene, as well as industrial chemicals like PCBs, and the unwanted waste by-products polychlorinated dibenzo-p-dioxin and dibenzofurans (PCDD/F), and brominated flame retardants [75]. These chemicals have common, but distinct chemical and physical characteristics including:

- POPs 'persist' in a certain environment resisting physical, chemical and/or biological processes of break-down;
- POPs are transported via air/water currents over long distances because they are semi-volatile causing them to evaporate slowly and enter the atmosphere. They then return to earth in rain and snow in colder areas leading to accumulation in regions such as the Arctic which is thousands of kilometres away from their source;

- POPs have adverse effects in human and animal tissue even at very low concentrations. Some of these compounds disrupt normal biological functions, including hormone and other chemical messengers leading to metabolic conditions [79];
- POPs have a low water and high lipid solubility, resulting in bio-accumulation in the fatty tissue of living organisms and cannot be excreted readily. Also, bio-magnification occurs causing an accumulation effect by factors of many thousands or even millions, as these compounds move up food chains [74, 77, 80, 82].

These chemical compounds are primarily products and by-products of industrial processes, synthetic chemical manufacturing and waste incineration ([80, 81]. Their existence dates back to the industrial boom after World War II, but are currently ubiquitous, and are found in food as well as soil, the atmosphere and various water bodies. In 2001, the United Nations Environment Program (UNEP) completed global negotiations with the signing of the so-called Stockholm convention on banning certain POPs, collectively known as the 'dirty dozen'. During this assessment, certain criteria for the identification and listing of chemicals under the convention were identified. New POPs that were identified during the survey include butylated tin, methylated mercury and polyaromatic hydrocarbon (PAH), as well as other less studied compounds such as chlorinated paraffin's, brominated diphenyl ethers and other flame retardants.

The big concern caused by organo-chlorines is because of growing evidence that these compounds act as endocrine disruptors [79, 83]. The U.S. EPA [83] report defined endocrine disruptors as 'exogenous agents that interfere with the synthesis, secretion, transport, binding, action or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development and/or behaviour'. The science of endocrine disruption is still very new (only about 2 decades) and long term studies with effect results are therefore still preliminary [80]. The hormone disrupting effects differ according to the exposure situation and depend on the relative occurrence of the active congeners, specifically on the trophic level from which the food originates. For example, contaminants in the marine food chain of the Arctic Inuit population follow a very long passage. The result is that the higher, slowly metabolized, higher chlorinated PCBs will dominate over the lower chlorinated and more readily metabolized congeners. This situation will therefore create a specific effect on the hormonal balance, which will be different from other populations exposed more directly to the sources of these contaminants [76]. Toxic contaminants can also act as causal or aggravating factors in the development of a range of metabolic disorders. Several studies reported a correlation between metabolic disorders such as diabetes and cardiovascular disease, and lipid adjusted serum levels of substances like PCBs and dioxins. At present, 80% of the adult Greenlandic human population has PCB serum values in excess of 10 μg/l; a concentration shown to cause increased incidences of diabetes. Processes related to the development of metabolic disorders in which toxic contaminants may play an aggravating role include: (1) Pro-inflammatory effect through the formation of pro-inflammatory cytokines, oxidative stress and/or the formation of reactive oxygen species, (2) modulation of fatty acid metabolism, (3) influence on nuclear receptors, (4) effects on steroidogenesis, and (5) influence on uric acid levels [76].

In cetaceans, POP pollution has been documented to cause a variety of species-specific and congener-specific toxic and physiological effects. These include the formation of cancers, reproductive and endocrine impairment, skeletal anomalies, immune-suppression, as well as organ-specific disorders [1, 79, 84]. Also, the POP effects are often not seen in the exposed generation but rather in the second or third generation offspring [83, 85]. Since these compounds are lipophilic, they accumulate in the blubber of cetaceans and other marine mammals [84]. In cetaceans, PCBs are a recognized immuno-suppressant and many researchers believe that high levels of these and other POPs reduce resistance of these animals to disease due to their poor ability to metabolize these compounds [1, 58, 79, 84]. If contamination levels are high enough, it is possible for marine pollution to cause outright deaths of cetaceans. One such case was in the St. Lawrence Estuary in Canada where a marine reserve was established for a resident population of beluga whales. At the time of the article, about one beluga corpse was being washed up every week. These whales had signs of depressed immune systems, complications with digestive systems and carcinogenic tumours. Clinical testing revealed levels of contamination so high that the corpses had to be treated as toxic waste under the Canadian legislation [86].

6.4. Plastics

Plastics are widely used globally for packaging and storage, because they are relatively inexpensive, light weight, convenient and do not break easily. However, they also create widespread environmental concerns, because they are manufactured from petroleum, which is a non-renewable and usually imported resource [87]. Moreover, plastics degrade very slowly, resulting in alarming volumes ending up in landfills and the marine environment. Plastics also present a health hazard. Cooking and storing food in plastic containers cause migration of chemicals, such as Bisphenol A (BPA), into food and beverages. Types of plastics that have been shown to leach these substances are polycarbonate, polyvinyl chloride (PVC) and styrene. Interestingly, the leaching effect increases with heating, freezing and contact with oily or fatty food. A number of studies revealed evidence that human and wildlife populations are exposed to levels of BPA high enough to cause harmful developmental and reproductive effects in a number of species and laboratory animal studies [88]. Canada's government ruled in April 2008 that BPA is harmful to infants and toddlers and announced plans to ban certain products. Some states in the USA are also considering bills to restrict or ban BPA from children's products (Reuters, 14 September 2008). However, after considering extensive research, the European Commission concluded (2008) that products containing BPA were safe for consumers, as long as the products were used as indicated by the manufacturer. In Canada, a ban on the importation, sale and advertising of polycarbonate baby bottles was enforced, together with implementation of efforts to reduce levels of BPA in infant formula, to the lowest achievable concentrations. The use of water bottles, sport bottles, sport equipment, etc. was considered to be safe and exposure from these, regarded to be very low. However, BPA was listed as 'CEPA toxic' in Canada in October 2010, to allow Environment Canada to establish water quality standard to restrict BPA levels in effluent discharges to the environment [89]. BPA is a common component of wastewater entering the oceans [90-92].

7. Conclusions

Under natural conditions and in a pristine environment, cetacean skin usually acts as an effective barrier against the environment, as well as against potential pathogenic microbes. The relatively thick, keratin-rich skin provides a physical barrier against injury and penetration by pathogens, while immune cells of both the innate and adaptive immune system occur in the skin. Despite this seemingly formidable barrier numerous different skin lesions were reported on cetaceans all over the globe during past decades. Many microbial species, including known pathogens, were found to be associated with the lesions. Viruses, bacteria and fungi were frequently encountered in the lesions, which seems to be more prevalent among immuno-compromised cetacean populations, and those subjected to pollution.

Typical toxic pollutants that enter the coastal waters via urban effluents all over the globe are heavy metals, POPs and plastics. The detrimental effects of these toxins on mammalian physiology are well known and include neuro-toxic effects, endocrine disruption, harmful effects on the reproductive system, as well as an impaired immune system. The latter would render mammals, including cetaceans, more susceptible to microbial infections. Moreover, taking into account that the large volumes of sewage effluents entering the oceans contain opportunistic pathogens, such as keratinophilic fungi, the development of skin lesions on a cetacean with an already compromised immune system as a result of toxic pollutants, seems inevitable.

Numerous case studies were reported where skin lesions were found on cetaceans from polluted waters. However, a clear connection between pollution levels and lesion incidence based on sound statistical analyses was not established. Nevertheless, surveys conducted on similar dolphin populations subjected to different levels of pollution, indicated that skin lesions among these animals were more prevalent in populations subjected to a polluted environment. Considering these results, together with known physiological effects of toxic pollutants, skin lesions among cetaceans may be indicative of an ecosystem under severe pressure as a result of anthropogenic activities. Since pollution levels are increasing in all the oceans of the world, it is imperative that more correlations between cetacean skin lesions and pollution levels be expediently studied on ecosystem, organismal, cellular and sub-cellular levels. The findings of such studies can be used by decision makers to manage anthropogenic activities, in such a manner that pollution to the marine environment is reduced for a sustainable planet.

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